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10/534,575	06/05/2006	Paul Wentworth	1361.027US2	3392

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EXAMINER	
ARCHIE, NINA	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,575	WENTWORTH ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,23,25,26,29,30 and 32-34* is/are pending in the application.

4a) Of the above claim(s) *1-20,31 and 35-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21,23,25,26,29,30 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on February 18, 2009 has been entered.

Amendment Entry

2. The amendment filed February 18, 2009 has been entered. Claims 1-21, 23, 25-26, 29-30, and 32-34 are pending. Claim 21 has been amended. Claims 1-20, 31 and 35-47 are withdrawn as being drawn to non-elected inventions. Claims 21, 23, 25-26, 29-30, and 32-34 are currently under examination.

Rejections Withdrawn

3. The new matter rejection of claims 21, 23, 25-26, 29-30 and 32-34 under 35 U.S.C. 112, first paragraph has been withdrawn in view of applicants amendments and arguments.

Response to Arguments

4. Applicant's arguments with respect to claims, 23, 25-26, 29-30, and 32-34 have been considered but are moot in view of the ground(s) of rejection.

Claim Rejections Maintained - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Examiner interprets claim 21 as a method for treating bacterial infection via production of ozone in a mammal comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can

generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody.

5. The rejection of claims 21, 23, 25-26, 29-30, 32-34 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement are maintained for the reasons stated in the previous office action. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Applicant arguments:

Applicants arguments filed in response to the 35 U.S.C. 112, first paragraph, February 18, 2009 is carefully considered, but not found to be persuasive for the reasons below.

A) Applicants argue, the Examiner did not provide any specific reasoning as to why the claimed invention is not described in the specification and instead, the reasoning advanced by Examiner appears to be directed to whether a skilled artisan would be able to carry out the claimed invention. Applicants note that the Examiner has apparently confused the written description requirement with the issue of enablement and therefore, Applicants will address the Examiner's other reasoning in maintaining the instant rejection below together with the enablement rejection.

B) Applicants state as explained in the Applicants' previous response, "the subject specification has adequately disclosed and described the claimed invention to the extent it is directed to the genus of bacterial infections. Bacterial infections per se are not Applicants' invention. Instead, bacterial infections are all well known in the art. Therefore, the written description requirement does not demand an exhaustive list of all bacterial infections that might be encompassed by the claimed invention. Nevertheless, the subject specification does provide an extensive disclosure and representative numbers of bacterial infections suitable for the claimed methods (see, e.g., pages 25-26)." Applicants state in addition to the recited genus of bacterial infections, the subject specification has provided extensive description of how to

generate reactive oxygen species such as ozone *in vivo* to kill or inhibit the growth of bacteria, including how to providing antibody activity, sources of singlet oxygen, and methods of evaluating anti-microbial activity and effective dosages. Applicant's state for example, antibodies to be administered to a subject are described in the specification, e.g., at page 20, 2nd full paragraph; page 21, 2nd and 3rd paragraphs; page 22, 4th paragraph; page 26, 3rd full paragraph; and pages 29-37. Applicants state antibody-catalyzed generation of reactive oxygen species and sensitizer molecules used therein are described in the specification, e.g., at page 21, 1st and 4th paragraphs; and page 23, 2nd to 5th paragraphs and in addition, pharmaceutical compositions comprising an antibody, as well as administration routes and dosages thereof, are also described in the specification (e.g., pages 37-41). Applicants state the specification further provides more detailed guidance and specific procedures for practicing the present invention with exemplified bacterial species such as Escherichia and Salmonella (see, e.g., Examples III and IV).

In response to (A), the specific reason as to why the claimed invention is not described and the written description is maintained because the claims are drawn a genus of antibodies that kill bacteria via ozone when in the presence of singlet oxygen. The specification lacks disclosure of vast genus of antibodies that posses the activity of killing bacteria via the production of ozone.

In response to (B), the basis of the rejection is the specification's failure to adequately describe antibodies that kill bacteria via the production of ozone in the presence of singlet oxygen. The specification discloses antibodies to be administered to a subject in the (e.g., at page 20, 2nd full paragraph; page 21, 2nd and 3rd paragraphs; page 22, 4th paragraph; page 26, 3rd full paragraph; and pages 29-37). The specification discloses antibody-catalyzed generation of reactive oxygen species and sensitizer molecules (e.g., at page 21, 1st and 4th paragraphs; and page 23, 2nd to 5th paragraphs) and pharmaceutical compositions comprising an antibody, as well as administration routes and dosages thereof (see e.g., pages 37-41). However the specification has only disclosed a limited number of antibodies that possess the activity of killing bacteria via the production of ozone which is not representative of the genus. Moreover, the specification provides detailed guidance and specific procedures with exemplified bacterial species such as Escherichia and Salmonella (see, e.g., Examples III and IV) but the lack of

written description to antibodies that possess the activity of killing bacteria via the production of ozone for practicing the present invention is not disclosed in the specification

Furthermore, the specification only discloses murine monoclonal antibody IgG and sheep polyclonal antibodies IgG that kill bacteria via the production of ozone (see pgs. 77-80). Therefore the murine monoclonal antibody IgG and sheep polyclonal antibodies IgG antibodies satisfy the written description requirements but are not representative of the claimed genus.

The specification discloses an antibody contemplated for use in the present invention can be in any of a variety of forms, including a whole immunoglobulin, Fv, Fab, F(ab').sub.2 other fragments, and a single chain antibody that includes the variable domain complementarity determining regions (CDR), or other forms. The specification states the present invention contemplates the use of any specificity of an antibody, polyclonal or monoclonal, and is not limited to antibodies that recognize and immunoreact with a specific antigen (see 0119). The specification discloses that most antibodies don't kill directly but merely tag a pathogen for other immunological processes (see background section of specification pg. 1).

Therefore the limited number of antibodies disclosed in the specification is not properly described. The limited number of species disclosed is not deemed to be representative of the genus encompassed by the instant claims. Moreover, Applicant is reminded that adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

As outlined previously, the claims are drawn to a method of treating a bacterial infection via production of ozone in a mammal comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody.

To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of

the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention. To adequately describe the genus of the antibody, applicant must also give a functional limitation of which the antibody.

The specification, however, does not disclose distinguishing and identifying features of a representative member of the genus of antibodies to which the claims are drawn, such as a correlation between structure of the protein and its recited function, so that the skilled artisan could immediately envision or recognize at least a substantial number of members of the claimed genus of antibodies.

MPEP § 2163.02 states, "an objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Ink's. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5,2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (ld. at 1104).

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing

only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus.

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. According to Greenspan et al., an epitope will include residues that make contacts with a ligand, here the antibody, but are energetically neutral, or even destabilizing to binding. Moreover, an epitope will not include any residue not contacted by the antibody, even though substitution of such a residue might profoundly affect binding. Accordingly, it follows that the immunoepitopes that can elicit a protective immune response to a given pathogen can only be identified empirically.

As stated earlier, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. The possible structural variations are limitless to any class of bacterial infections that can be treated, and antibodies and microbes that can be used. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any specific examples of any type of bacterial infection treated with the product of an anti-microbial composition as claimed, the specification is void of any method of treating any type of bacterial infection to produce ozone production. The written description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir.
1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Therefore, absent a detailed and particular description of a representative number, or at least a substantial number of the members of the genus antibodies the skilled artisan could not immediately recognize or distinguish members of the claimed genus of antibodies. Therefore, in accordance with the Guidelines, the description of the antibodies is not deemed representative

of the genus of the antibody of the claimed invention thus the claims does not meet the written description requirement.

6. The rejection of claims 21, 23, 25-26, 29-30 and 32-34 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contain subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant arguments:

Applicants arguments filed in response to the 35 U.S.C. 112, first paragraph, February 18, 2009 is carefully considered, but not found to be persuasive for the reasons below.

Enablement provided by the subject disclosure

A) Applicants state the presently claimed invention is directed to methods of treating bacterial infection in a mammal via administering an antibody and a sensitizer molecule so that ozone is produced to exert the antimicrobial activity. To simplify the analysis, the issue of whether the claimed methods are enabled can be broken down to (i) enablement of administration of the recited antibody and the sensitizer molecule; (2) enablement of production of ozone by the administered antibody and the sensitizer molecule; and (3) enablement of bactericidal activity of ozone.

First, the claimed methods require the administration of an antibody and a sensitizer molecule to a mammal in need of treatment for bacterial infection. As clarified above, antibodies and sensitizer molecules suitable for the invention are taught in great detail in the specification. The specification also disclosed that the administered antibody can be specific for the target microbe (see, e.g., page 22, third paragraph). Thus, for any given target bacterium, one can readily select an antibody that recognizes a surface antigen of the bacterium. For example, the antibody can be one that recognizes lipopolysaccharide (the common antigen present in the outer membrane of Gram-negative bacteria) or one that recognizes peptidoglycan (a common antigen present in Gram-positive bacteria and also in Gram-negative bacteria at lower levels). Such

antibodies are all well known and routinely used in the art (see, e.g., USPN 6,315,999; and Bokisch et al., J. Exp. Med. 138: 1184-93, 1973). Similarly, various sensitizer molecules are also known in the art, with some specific exemplification set forth in the specification (e.g., page 23). It is readily apparent that these materials (i.e., the recited antibody and the sensitizer) can be readily obtained commercially or generated in accordance with the subject disclosure or knowledge well known in the art.

B) Applicants state, that second, antibody-catalyzed production of reactive oxygen species (including ozone) in vivo from a source of singlet oxygen (e.g., a sensitizer molecule) is undoubtedly also enabled in the present application and this element of the claimed invention is the essence of the scientific findings from which the invention is derived. Applicants state, throughout the specification, it was taught that antibodies have the intrinsic ability to catalyze the conversion of singlet oxygen into reactive oxygen species. Applicants state that the specification also taught and experimentally demonstrated that ozone is produced by isolated antibodies (e.g., page 82) or antibodies on activated neutrophils (e.g., at page 85). Applicants state the specification additionally exemplified bacterial killing with antibody-generated reactive oxygen species against E. coli and S. typhimurium (see, e.g., Examples 3-4). Applicants state that these disclosures clearly demonstrated that bactericidal activity can be derived from antibody-catalyzed ozone production.

C) Such a broad-spectrum antimicrobial activity is unequivocally taught in the art. Applicants state that for example, as noted in one of the references cited by the Examiner, Sunnen (pgs. 1-4, Ozonics International, 2005), the inhibitory and lethal effects of ozone on noxious organisms have been observed since its discovery by Schonbein in 1840…" Consistently, there have been numerous reports in the art of ozone-mediated killing of various bacterial species, e.g., Escherichia coli, Bacillus cereus, Bacillus megaterium, coliform bacteria, Staphylococcus aureus, and Aeromonas hydrophilia. See, e.g., Broadwater et al., Appl. Microbiol. 26:391-3, 1973; Burleson et al., Appl. Microbiol. 29:340-4, 1975; Dyas et al., J. Clin. Pathol. 36:1102-4, 1983; and Lohr et al., J. Aquaric. Aquat. Sci. 4:1-8, 1984. Admittedly, these prior art studies did not employ a system of antibody-generated ozone production as presently claimed. However, the chemical nature and biological activity of ozone produced from the

antibody-catalyzed reaction as presently disclosed are surely the same as that of the ozone employed in the prior art studies.

D) Applicants state it is acknowledged that the subject specification did not actually exemplify the claimed methods in a mammal subject. Instead, according to the MPEP, data obtained from in vitro studies can provide enablement for a claimed in vivo method if there is a correlation between the in vitro data and the claimed methods (see MPEP § 2164.02). In addition, it is the Examiner's burden to ~give reasons for a conclusion of lack of correlation for an in vitro or in vivo animal model (MPEP § 2164.02). Thus, the issue in the instant case is whether the in vitro data demonstrating antibody-catalyzed ozone production and the accompanying bactericidal activity are reasonably correlated with an in vivo application as claimed. Applicant states that the Examiner has not advanced any convincing reasoning or evidence to show that such a correlation does not exist in the present case. To address this issue, the Examiner is advised to focus on the fact that the claimed invention is dependent on (i) the intrinsic catalytic activity underlying antibody-catalyzed ozone production, (2) the broad spectrum bactericidal activity of ozone due to its chemical nature. This intrinsic activity of antibodies and the chemical nature of ozone strongly suggest that the in vitro exemplification can be reasonably extrapolated into an in vivo setting as presently recited. Such an extrapolation is also supported by the disclosed data that antibodies on activated neutrophils can produce ozone with bactericidal activity (see, page 85 in Example 3).

In response to (A)., the specification discloses that an antibody can be specific for the target microbe (see, e.g., page 22, third paragraph) and thus, for any given target bacterium, one can readily select an antibody that recognizes a surface antigen of the bacterium. Furthermore Examiner agrees there are various sensitizer molecules are also known in the art. However the instant claims are drawn to method of treating a bacterial infection **via production of ozone in a mammal** comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody. The specification does not provide guidance regarding which

antibodies against a given bacterial pathogen generate ozone in the presence of a given sensitizer or whether said antibodies would have any efficacy *in vivo*.

In response to (B), The specification discloses antibodies have the intrinsic ability to catalyze the conversion of singlet oxygen into reactive oxygen species which is known in the art. Furthermore the specification discloses references that experimentally demonstrated that ozone is produced by isolated antibodies (e.g., page 82). The specification also discloses antibodies on activated neutrophils (e.g., at page 85) and bacterial killing with antibody-generated reactive oxygen species against E. coli and S. typhimurium (see, e.g., Examples 3-4). However, one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of a successful method for treating any bacterial infection in a mammal with any antibody and sensitizer molecule to produce ozone in view of the of general guidance in the specification and known unpredictability associated with the ability to predict anti-microbial composition will exert effects of ozone in any mammal. Applicants are speculating that one skilled in the art can administer the antimicrobial composition aforementioned to a mammal treating bacterial infection. The data in the specification does not support this assertion. Furthermore the data does not support that every antibody and sensitizer molecule will work equivalently or even work at all or that it is possible that some rare antibodies and sensitizer might not work at all in treating bacterial infection in a mammal. Furthermore, even though data in the specification discloses a given antibody produces ozone *in vitro*, the data is not indicative of ozone production resulting in the killing of a bacteria and no demonstration that said ozone production results in the killing of a bacteria in the specification. Also only bactericidal data demonstrated that a level of at least 5micromolar was required to achieve an effect which questions how the concentration is achieved *in vivo?* The specification is silent and lacks guidance as to how this concentration is achieved *in vivo*. Also the *in vitro* conditions do not reflect physiological conditions (experiment done at 4 degrees C (see 0328) as opposed to a physiological temperature. The specification does not provide guidance regarding which antibodies against a given bacterial pathogen generate ozone in the presence of a given sensitizer or whether said antibodies would have any efficacy *in vivo.* As a result of the lack of

guidance in the specification, and no correlation in the specification and the instant claims, one of skill in the art would consider the experimentation undue.

In response to (C), Applicant is reminded that the instant claims are not drawn to antimicrobial activity but a method of treating a bacterial infection in a mammal. Also, the instant claims are drawn to treating any and all bacterial infections, not just the isolated species disclosed in said references. Hence, the references as set forth supra do not provide any support with regard to the enablement of the instant invention. Furthermore the art does not indicate an antibody and sensitizer unconjugated to treat bacterial infection. Additionally the art does not indicate that hematoporphyrin as sensitizer molecule and an antibody can be used to treat bacterial infection. As stated in the previous office action, 11/25/2008, the state of the art is unpredictable with regard to the instant claims.

In response to (D), it is noted that Applicants state it is acknowledged that the subject specification did not actually exemplify the claimed methods in a mammal subject. In regards to Applicants stating the MPE (2164.02) and the specification disclosing in vitro data on bactericidal activity, there is no correlation between in vivo and vitro example of the instant method. As stated as set forth supra, Applicants are speculating that one skilled in the art can administer the antimicrobial composition aforementioned to a mammal treating bacterial infection. The data in the specification does not support this assertion. As set forth supra, even though data in the specification discloses a given antibody produces ozone *in vitro*, the data is not indicative of ozone production resulting in the killing of a bacteria and no demonstration that said ozone production results in the killing of a bacteria in the specification. Also only bactericidal data demonstrated that a level of at least 5micromolar was required to achieve an effect which questions how the concentration is achieved *in vivo?* The specification is silent and lacks guidance as to how this concentration is achieved *in vivo*. Also the *in vitro* conditions do not reflect physiological conditions (experiment done at 4 degrees C (see 0328) as opposed to a physiological temperature.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (Where applicant claimed a composition suitable for the treatment of arthritis having a potency of "at least" a

particular value, the court held that the claim was not commensurate in scope with the enabling disclosure because the disclosure was not enabling for compositions having a slightly higher potency. Simply because applicant was the first to achieve a composition beyond a particular threshold potency did not justify or support a claim that would dominate every composition that exceeded that threshold value.); Further the scope of enablement must only bear a "reasonable correlation" to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

As outlined previously, the claims are drawn to a method of treating a bacterial infection via production of ozone in a mammal comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody.

The specification is not enabled for any method for treating bacterial infection via production of ozone comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody.

Enablement is considered in view of the *Wands* factors (MPEP 2164.01(a)).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

(A) The breadth of the claims;

(B) The nature of the invention;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims is very broad and the quantity of experimentation required is undue. The product being used to administer to a subject (human or otherwise) stated in claim 21, is overly broad. Claim 1 an antibody that can bind to any microbe and said antibody. Therefore it is hard for one skilled in the art to determine if the composition can be used in treating any type of bacterial infections in a mammal to yield the production of ozone. The quantity of experimentation required to practice the invention as claimed would require the de novo determination of accessible target sites, modes of delivery and formulations of the anti-microbial compositions to target appropriate cells and/or tissues in any and/or all organisms/subjects, and further whereby treatment effects are provided for the claimed conditions. Since the specification fails to provide particular guidance for administering an anti-microbial composition comprising any antibody that can bind to any microbe to produce ozone in a mammal for treatment of any bacterial infection, it would require undue experimentation to practice the invention over the broad scope as presently claimed.

Nature of the invention/The existence of working examples.

The claims are drawn to method of treating bacterial infection via production of ozone comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody, wherein said composition produces ozone in a mammal.

The state of the prior art is unpredictable with regard to microbial infection treatments comprising an antimicrobial composition as set forth supra. The state of the art teaches that Hasan et al teach a method of treating a subject, for a disorder characterized by the presence of an unwanted organism such as Salmonella, comprising: administering to the subject a conjugate comprising a polylysine backbone to which is coupled a targeting moiety and a porphyrin photosensitizer such as a hematoporphyrins (see claims, section "Phostosensitizers" Hasan et al US Patent 7,268,155 September 2007). The art indicates that Goers et al teach an antibody-therapeutic agent conjugate, comprising: a therapeutic agent capable of acting as a photothermolytic agent, as a photosensitizer to mediate cytotoxic effects nearby cells are mediated through the generation of singlet oxygen molecules and oxygen free radicals (see claims abstract, Section 3 Summary of Invention paragraphs 1-4, see section 7 see Goers et al WO 1986/001720 March 1986 in its entirety). The art indicates that Wentworth et al teach that antibodies to convert molecular oxygen into hydrogen peroxide, thereby effectively linking recognition and killing events (see abstract). Wentworth et al teach that irradiation of antibodies with visible light in the presence of a known photosensitizer of ozone in aqueous solutions, hematoporphyrin, leads to hydrogen peroxide formation (see column 2 paragraph 2). Thus Wentworth et al teach reactive oxygen species is hydrogen peroxide.

The art indicates ozone in the body may have a protective role against pathogenic invaders. The art indicates reactive oxygen species (ROS) (hyroxyl radical, nitric oxide, and hydrogen peroxide) produced by immune system cells during infectious processes. The art indicates the crucial role of ozone in the task of staving off invading microorganisms had not been as fully explained in under-publicized article with momentous implications (Wentworth et al 2002) documented that ozone is indeed produced in the body in the context of immune function. The art indicates antibodies, provided with appropriate starting materials, are capable of creating singlet oxygen, a most powerful oxidant. The art indicates ozone in combination with hydrogen peroxide, could account for the inactivation of 95% of Escherichia coli bacteria, ozone thus becomes a pivotal factor for fighting microorganisms. The art indicates that ozone functions as a signaling agent by stimulating production of nuclear factor kappa B, interleukin 6, and tumor necrosis factor a. The art indicates ozone is a strong bactericide needing only a few micrograms per milliliter for measurable action at a concentration of 1 mg/liter H2O, ozone

rapidly inactivates bacteria (See Sunnen pgs. 1-4 Sunnen see Gerald. Ozonics International Copyright 2005 in its entirety). The art indicates a partial list of organisms susceptible to ozone inactivation includes both aerobic and anaerobic bacteria. The art indicates while exogenously applied ozone has received total investigative focus, little or no attention has been paid to endogenously generated ozone. The art indicates ozone has been seen as a molecule capable of inducing the formation of reactive oxygen species but not as a molecule specifically produced by the body to fight infection and ozone in the task of staving off invading microorganisms and not as a molecule specifically produced by the body to fight infections (See Sunnen pgs 1-4). The art indicates research is compellingly needed to understand the deeper mechanisms of ozone and nitric oxide formation in the immune system so that novel antimicrobial therapies may be recruited to respond to the world's increasingly urgent public health needs (See Sunnen pgs 1-4). The art has not shown any anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein said composition produces ozone in a mammal for treating bacterial infection. For the reasons set forth supra, the state of the art is unpredictable with regard to treating any bacterial infection.

Guidance in the specification. The specification discloses Examples of antibodies that have the capacity to destroy antigens and Microbiocidal action against Salmonella typhimurium. The specification teaches the bactericidal activity of the antibody and source of singlet oxygen within an in vitro assay. Moreover, example IV teaches said activity towards Salmonella, wherein the inhibition of growth occurred during the in vitro portion (see pp. 45-88). The specification does not give an example of an antimicrobial composition to treat bacterial infections. The examples disclose in the specification only contemplate the claimed invention. The specification provides little guidance regarding how the antimicrobial composition as set forth supra is effective when treating bacterial infections and further more how the anti-microbial composition as claimed will produce ozone in a mammal for treating a bacterial infection. Therefore one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of the successful treatment in any mammal by production of ozone. The specification as filed fails to provide particular guidance which

resolves the known unpredictability in the art associated with effects provided upon administration via any route.

In conclusion, the claimed inventions are not enabled for any method for treating bacterial infection via production of ozone comprising administering to the mammal an anti-microbial composition consisting essentially of an antibody that can bind to a microbe, a sensitizer molecule that can generate singlet oxygen and a pharmaceutically acceptable carrier, wherein the sensitizer molecule is not conjugated to the antibody. Furthermore, the specification does not give an example of an antimicrobial composition to treat bacterial infections. The examples disclose in the specification only contemplate the claimed invention. The product being used to administer to a mammal stated in claim 21, is overly broad. The state of the art is unpredictable to administer antimicrobial composition to treat bacterial infections and produce ozone in a mammal. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed methods.

Conclusion

7. No claims allowed.
Claims 21, 23, 25-26, 29-30, 32-34 are rejected and under examination.
Claims 22, 24, and 27-28 have been cancelled.
Claim 1-20, 31, 35-47 are withdrawn.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/
for Nina Archie, Examiner of Art Unit 1645